

## EXHIBIT 2

8/4/2005

Enzon Pharmaceuticals Inc. v. Phoenix Pharmacologics  
Confidential Pursuant To Protective Order

David Filpula

Page 1

1 IN THE UNITED STATES DISTRICT COURT

2 FOR THE DISTRICT OF DELAWARE

3 -----

4 ENZON PHARMACEUTICALS, INC.,

5 Plaintiff,

6 Civil Action No  
- against - 04-1285 (GMS)

7

8 PHOENIX PHARMACOLOGICS, INC.,

9 Defendant.

10 -----

11 9:00 a.m.

12 August 4, 2005

13 One Broadway

14 New York, New York

15

16 CONFIDENTIAL

17 VIDEOTAPED DEPOSITION of DAVID RAY  
18 FILPULA, a Witness in the above entitled  
19 matter, taken pursuant to Rule 30(b)(6), before  
20 Stephen J. Moore, a Registered Professional  
21 Reporter, Certified Realtime Reporter, and  
Notary Public of the State of New York.

20

21 -----

22 DIGITAL EVIDENCE GROUP

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<p style="text-align: right;">Page 166</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 discussions about using higher molecular weight</p> <p>3 PEGs with ADI, whether we were talking about 35</p> <p>4 or 45 or 40, I wouldn't remember that level of</p> <p>5 detail.</p> <p>6 Q These general discussions to</p> <p>7 which you have referred, did they involve Dr.</p> <p>8 Clark?</p> <p>9 MR. SIEM: Objection to form.</p> <p>10 A I'm not certain, but since he</p> <p>11 was a member of the ADI sourcing team, was</p> <p>12 invited to all the meetings, contributed to the</p> <p>13 discussion at the meetings when he attended and</p> <p>14 was provided with all documents and information</p> <p>15 pertaining to PEG and ADI, I would think that</p> <p>16 he would be likely to be included in such</p> <p>17 discussions.</p> <p>18 Q Where did Dr. Clark get the idea</p> <p>19 of using PEG 40,000 with ADI as referenced in</p> <p>20 the '738 patent?</p> <p>21 MR. SIEM: Objection to form.</p> <p>22 A Well, I cannot be a mind reader</p> <p>23 and be certain in what somebody else was</p> <p>24 thinking.</p> <p>25 I believe that the work that we</p>	<p style="text-align: right;">Page 168</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 experiment that you think about, resources are</p> <p>3 limited.</p> <p>4 Q And they were limited at Enzon,</p> <p>5 right?</p> <p>6 MR. SIEM: Objection to form.</p> <p>7 A They are limited everywhere.</p> <p>8 Q But evaluating higher molecular</p> <p>9 weight --</p> <p>10 MR. LUCCI: Let me strike that.</p> <p>11 Q But evaluating PEG-ADI having</p> <p>12 PEG polymers of molecular weight greater than</p> <p>13 12,000 wasn't something that was evaluated at</p> <p>14 Enzon, was it?</p> <p>15 A I can't be sure of that, I</p> <p>16 already found a listing in one of our</p> <p>17 manuscripts suggesting that we may have looked</p> <p>18 at a 24K PEG.</p> <p>19 I'm not certain of the total</p> <p>20 list of compounds that may have been explored</p> <p>21 to some level in looking at and investigating</p> <p>22 the properties that PEGylated ADI compounds.</p> <p>23 One does not necessarily do a</p> <p>24 thorough evaluation, meaning both biochemical</p> <p>25 and cell culture and animal study type data,</p>
<p style="text-align: right;">Page 167</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 conducted in our PEG-ADI program at Enzon</p> <p>3 showed that the higher molecular weight PEGs</p> <p>4 performed better and therefore it would teach</p> <p>5 us as a team that the use of the higher</p> <p>6 molecular weight PEGs is a good thing.</p> <p>7 Q Well, if it was taught to the</p> <p>8 folks at Enzon the higher molecular weight PEG</p> <p>9 is a good thing, how come we haven't seen any</p> <p>10 documents in which that was actually explored?</p> <p>11 MR. SIEM: Objection to form.</p> <p>12 A In my view we did see such a</p> <p>13 document in our manuscript, for one example we</p> <p>14 show that the 12K outperformed the 5K.</p> <p>15 Q Well, if it's taught to the team</p> <p>16 that higher molecular weight is better,</p> <p>17 wouldn't the logical extension of that be to go</p> <p>18 even higher than 12?</p> <p>19 MR. SIEM: Objection to form.</p> <p>20 A I think that that would be</p> <p>21 something that a scientist would think about</p> <p>22 and evaluate, at least in his thoughts, and</p> <p>23 perhaps want to follow-up on in</p> <p>24 experimentation.</p> <p>25 You can't always do every</p>	<p style="text-align: right;">Page 169</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 one may stop at a preliminary testing where the</p> <p>3 question is asked how does this particular PEG</p> <p>4 or linker affect the specific activity of the</p> <p>5 conjugate, and if time and the cost don't allow</p> <p>6 us to explore every single compound, we may not</p> <p>7 be able to go further with every single</p> <p>8 compound to the more extensive and thorough</p> <p>9 investigation involving these animal and cell</p> <p>10 culture models.</p> <p>11 Q Dr. Filpula, can you point me to</p> <p>12 a single document in Enzon's document</p> <p>13 production to Phoenix where the use of PEG</p> <p>14 having a molecular weight of 40,000 is</p> <p>15 discussed in connection with PEGylating ADI?</p> <p>16 MR. SIEM: Objection to form.</p> <p>17 A In the documents that I reviewed</p> <p>18 the past few days, I don't recall seeing that</p> <p>19 specific example.</p> <p>20 That doesn't mean there might</p> <p>21 not be information on that contained in the</p> <p>22 relative documentation that is part of this</p> <p>23 litigation.</p> <p>24 There is certainly a great deal</p> <p>25 of work that has been done with 40K PEG at</p>

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<p style="text-align: right;">Page 170</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 Enzon on various compounds, therefore</p> <p>3 exploration of that at Enzon per ADI would not</p> <p>4 surprise me, I just do not see any specific</p> <p>5 examples of that contained in the documents</p> <p>6 that I reviewed the last few days.</p> <p>7 Q Is PEG of 40,000 molecular</p> <p>8 weight -- let me just phrase it differently,</p> <p>9 are PEGs of molecular weight greater than</p> <p>10 24,000 proprietary to Enzon?</p> <p>11 MR. SIEM: Objection to form.</p> <p>12 A That may depend upon several</p> <p>13 factors, it would, perhaps, depend upon the</p> <p>14 linker employed, it may depend upon the design</p> <p>15 of the PEG, such as whether one uses a branch</p> <p>16 structure or not.</p> <p>17 There may be other factors.</p> <p>18 Q Well, the claim here that we</p> <p>19 were looking at in the '738 patent just talks</p> <p>20 about polyethylene glycol having a total weight</p> <p>21 average molecular weight of from about 1,000 to</p> <p>22 about 40,000.</p> <p>23 Now, polyethylene glycol having</p> <p>24 a total weight average molecular weight of</p> <p>25 about 40,000 had been in the literature before</p>	<p style="text-align: right;">Page 172</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 wide array of different sizes of PEGs for any</p> <p>3 protein would be very usual.</p> <p>4 Q Now, looking at the remainder of</p> <p>5 claim 1 in the '738 patent, you see there the</p> <p>6 portion of claim 1 that appears in column 20,</p> <p>7 do you see that there begins with the word</p> <p>8 linking group?</p> <p>9 A Yes.</p> <p>10 Q And it says, continuing from the</p> <p>11 prior paragraph, says, "Wherein the linking</p> <p>12 group is selected from the group consisting</p> <p>13 of," do you see that language?</p> <p>14 A Yes.</p> <p>15 Q Now, the first linking group</p> <p>16 that's listed there is a succinamide?</p> <p>17 A Yes.</p> <p>18 Q The next one is an amide group,</p> <p>19 right?</p> <p>20 A Yes.</p> <p>21 Q Are you aware of any document</p> <p>22 that has been produced to Phoenix in this</p> <p>23 litigation that discusses using an amide group</p> <p>24 to link a PEG molecule to ADI?</p> <p>25 MR. SIEM: Objection to form.</p>
<p style="text-align: right;">Page 171</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 1994, hadn't it?</p> <p>3 MR. SIEM: Objection to form.</p> <p>4 A Again, I would want to carefully</p> <p>5 examine that point with regard to the date you</p> <p>6 mentioned, but I think that PEGs of various</p> <p>7 sizes have been explored in the literature</p> <p>8 prior to 1994, including ones that are quite</p> <p>9 large.</p> <p>10 Q On the order of -- quite large</p> <p>11 meaning on the order of 40,000, correct?</p> <p>12 A Yes.</p> <p>13 Q Just for the record, your answer</p> <p>14 to my question was yes?</p> <p>15 A Yes.</p> <p>16 Q Just so we are clear on the</p> <p>17 record, you are not able to identify for me any</p> <p>18 discussion at Enzon relating to the use of PEG</p> <p>19 40,000 with ADI, is that correct?</p> <p>20 MR. SIEM: Objection to form.</p> <p>21 A I can't recall specific examples</p> <p>22 of conversations between particular individuals</p> <p>23 relating to that specific construction.</p> <p>24 But typically at Enzon</p> <p>25 conversations about modifying proteins with a</p>	<p style="text-align: right;">Page 173</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 A I will have to say that the</p> <p>3 language of claim 1 is a bit unclear to me in</p> <p>4 that the linking group could well be an amide.</p> <p>5 Typically the succinamide would</p> <p>6 be a leaving group and in a different formal</p> <p>7 chemical category from the actual linkage,</p> <p>8 which could be an amide.</p> <p>9 The -- it may be that the XUS</p> <p>10 linker that we referred to forms an amide</p> <p>11 linkage, I would have to doublecheck that,</p> <p>12 however that may also occur with the T PEG.</p> <p>13 The SC would generate what is</p> <p>14 called a carbamate or urethane linkage.</p> <p>15 Q Now, you see one of the groups</p> <p>16 listed there is an ester group?</p> <p>17 A Yes.</p> <p>18 Q Did you see any reference in the</p> <p>19 documents that have been produced to Phoenix in</p> <p>20 this litigation of using an ester group to link</p> <p>21 a PEG polymer to ADI?</p> <p>22 MR. SIEM: Objection to form.</p> <p>23 A I don't specifically remember</p> <p>24 that example. Ester groups are rather common</p> <p>25 in well-known PEG linkers, so it's something</p>

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<p style="text-align: right;">Page 174</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 that could easily be discussed at any time.</p> <p>3 Q Well, given that they are</p> <p>4 well-known, isn't it surprising that you didn't</p> <p>5 see them mentioned in any documents produced by</p> <p>6 Enzon?</p> <p>7 MR. SIEM: Objection to form,</p> <p>8 mischaracterizes the witness' testimony.</p> <p>9 A Again, the linkers that I recall</p> <p>10 seeing are ones that I've listed. There were,</p> <p>11 perhaps, a number of other linkers explored in</p> <p>12 our PEGylation program.</p> <p>13 The ester linkage actually is</p> <p>14 not regarded as the best strategy to use for</p> <p>15 PEGylation due to its instability.</p> <p>16 Q And the experiments you are</p> <p>17 referring to talking about the use of the ester</p> <p>18 linkage is with a molecule different from ADI,</p> <p>19 correct?</p> <p>20 A Yes, the general statement I</p> <p>21 made is a generalization, not specifically</p> <p>22 directed to ADI.</p> <p>23 Q Now, the next group here is an</p> <p>24 epoxy group, is there any document that's been</p> <p>25 produced to Phoenix in this litigation by Enzon</p>	<p style="text-align: right;">Page 176</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 the primary amines of lysines it's also able to</p> <p>3 react with cysteines and histadines, and</p> <p>4 tyrosines.</p> <p>5 Q But, Dr. Filpula, this is</p> <p>6 talking about the use of a succinamide linker</p> <p>7 as an alternative to a histadine, not together</p> <p>8 with a histadine, isn't it?</p> <p>9 MR. SIEM: Objection to form,</p> <p>10 calls for a legal conclusion.</p> <p>11 A I'm uncertain as to what</p> <p>12 specifically is referred to here. As I've</p> <p>13 noted previously, the language is a bit</p> <p>14 confusing in that there is a description of</p> <p>15 what typically would be a linkage, such as an</p> <p>16 amide, and description of what would typically</p> <p>17 be a linker, such as a succinamide.</p> <p>18 Q But if we focus on carboxyl</p> <p>19 groups, carboxyl groups, hydroxyl groups and</p> <p>20 carbohydrate groups, you're not aware of any</p> <p>21 document that Enzon has produced in this</p> <p>22 litigation, are you, that discusses the use of</p> <p>23 those groups to link ADI to a PEG polymer, are</p> <p>24 you?</p> <p>25 MR. SIEM: Objection to form.</p>
<p style="text-align: right;">Page 175</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 that refers to the use of an epoxy group to</p> <p>3 link ADI to a PEG polymer?</p> <p>4 MR. SIEM: Objection to form.</p> <p>5 A I don't specifically recall</p> <p>6 communication of that, again the epoxy group</p> <p>7 would be difficult to work with and probably</p> <p>8 not be a premier choice for PEGylation.</p> <p>9 Q Now, the remainder of that</p> <p>10 portion of claim 1 refers to a carboxyl group,</p> <p>11 a hydroxyl group, a carbohydrate, a tyrosine</p> <p>12 group, cysteine group, and a histadine group,</p> <p>13 do you see that?</p> <p>14 A Yes.</p> <p>15 Q Are you aware of any documents</p> <p>16 that Enzon has produced to Phoenix in this</p> <p>17 litigation that discuss the use of any of those</p> <p>18 linkers to link ADI to a PEG polymer?</p> <p>19 MR. SIEM: Objection to form.</p> <p>20 A And again, I'm not sure of the</p> <p>21 exact wording of that in documents that I have</p> <p>22 seen, but it would be relevant to one of the</p> <p>23 compounds that we explored and described in our</p> <p>24 work, for example the SC PEG compound, the SC</p> <p>25 linker, while it primarily reacts with lysines,</p>	<p style="text-align: right;">Page 177</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 A I don't recall specific examples</p> <p>3 of that in the documents that I've looked at</p> <p>4 recently.</p> <p>5 Nonetheless, one could envision</p> <p>6 ways that you could modify the ADI protein</p> <p>7 through different linker chemistries such that</p> <p>8 it could react with these moieties, the</p> <p>9 carbohydrate and carboxyl and hydroxyl groups,</p> <p>10 the approaches would be disclosed by various</p> <p>11 publications.</p> <p>12 Q Did Enzon ever link ADI to a PEG</p> <p>13 polymer using an Ester group, epoxy group,</p> <p>14 carboxyl group, hydroxyl group, carbohydrate</p> <p>15 group?</p> <p>16 MR. SIEM: Objection to form.</p> <p>17 A Again, the ones you listed were.</p> <p>18 Q Ester, epoxy, carboxyl,</p> <p>19 hydroxyl, carbohydrate?</p> <p>20 MR. SIEM: Same objection.</p> <p>21 A ADI does not have any</p> <p>22 carbohydrates, that is a bit confusing as to</p> <p>23 why that was included.</p> <p>24 The chemistries for hydroxyl and</p> <p>25 to some extent carboxyl and certain epoxy would</p>

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<p style="text-align: right;">Page 178</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 be not premier chemistries for this</p> <p>3 application.</p> <p>4 And I don't specifically</p> <p>5 remember exploration of those, although it's</p> <p>6 possible that those were included in our</p> <p>7 programs.</p> <p>8 I didn't run across specific</p> <p>9 mention of that in the documents that I</p> <p>10 reviewed.</p> <p>11 Q So, it's your understanding that</p> <p>12 Enzon definitely did any work using hydroxyl or</p> <p>13 epoxy groups to link ADI to a PEG polymer, is</p> <p>14 that correct?</p> <p>15 MR. SIEM: Objection to form,</p> <p>16 mischaracterizes the witness' testimony.</p> <p>17 A Rather I'm saying I don't know,</p> <p>18 however I've not seen that specific example in</p> <p>19 the recent documents I've reviewed.</p> <p>20 Q Dr. Filpula, do you recall any</p> <p>21 discussions at Enzon about using as a linker</p> <p>22 for PEG and ADI any of the ester, epoxy,</p> <p>23 carboxyl, hydroxyl or carbohydrate groups we</p> <p>24 have been discussing?</p> <p>25 MR. SIEM: Objection to form.</p>	<p style="text-align: right;">Page 180</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 molecular genetics, or possibly it was called</p> <p>3 the biology department reporting to Rob Schorr</p> <p>4 who was, I think, V.P. of research.</p> <p>5 His responsibilities were not</p> <p>6 only in PEG-ADI, he worked on at least one</p> <p>7 other major program as well.</p> <p>8 Within the ADI program he was a</p> <p>9 member of the ADI sourcing team and would have</p> <p>10 contributed to discussions at those team</p> <p>11 meetings, and invited to all the meetings, he</p> <p>12 would have received all the meeting minutes and</p> <p>13 information about the program, both the</p> <p>14 PEGylation and the ADI component.</p> <p>15 So his job was to serve as a</p> <p>16 communication link between the ADI sourcing</p> <p>17 team and senior management, as a top manager he</p> <p>18 had responsibilities in managing resources,</p> <p>19 making sure that we had enough people to do the</p> <p>20 job, enough money, enough equipment.</p> <p>21 He also had responsibilities in</p> <p>22 fostering the relationship between Enzon and</p> <p>23 Lloyd Old's lab at Ludwig.</p> <p>24 Q Now, you're not aware of anyone</p> <p>25 at Enzon discussing use of ester, epoxy,</p>
<p style="text-align: right;">Page 179</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 A I don't specifically recall the</p> <p>3 discussions about that.</p> <p>4 Q Did anyone at Enzon communicate</p> <p>5 the use of those groups as a linker for PEG and</p> <p>6 ADI to Dr. Clark?</p> <p>7 MR. SIEM: Objection to form.</p> <p>8 A I don't recall that.</p> <p>9 Q Did Dr. Clark work on those</p> <p>10 groups as linkers for PEG and ADI when he was</p> <p>11 at Enzon, and by those groups I mean ester,</p> <p>12 epoxy, carboxyl, hydroxyl and carbohydrate?</p> <p>13 MR. SIEM: Objection to form.</p> <p>14 A I'm sorry, could you read that</p> <p>15 question back?</p> <p>16 (The question requested was read</p> <p>17 back by the reporter.)</p> <p>18 A No, I don't recall that at all.</p> <p>19 Mike wasn't a PEGylation expert. He didn't do</p> <p>20 PEGylation work at Enzon.</p> <p>21 Q What type of work did Dr. Clark</p> <p>22 do at Enzon?</p> <p>23 A Mike was an associate VP, his</p> <p>24 job was administrative and supervisory.</p> <p>25 He, I believe, headed the</p>	<p style="text-align: right;">Page 181</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 carboxyl, hydroxyl or carbohydrate groups to</p> <p>3 link PEG and ADI, correct?</p> <p>4 MR. SIEM: Objection to form.</p> <p>5 A I'm not -- I'm not familiar with</p> <p>6 using those chemistries, I think I remember</p> <p>7 them all, for the purpose of PEGylating ADI.</p> <p>8 Q So your testimony is you do</p> <p>9 remember them all for the purpose of</p> <p>10 PEGylating?</p> <p>11 A No, what I said was I do not</p> <p>12 remember the use of those linkers that you</p> <p>13 mentioned, the epoxy, the carbohydrate, I think</p> <p>14 you said carboxyl, hydroxyl, I don't recall</p> <p>15 work using those linkages specifically for</p> <p>16 PEGylating ADI.</p> <p>17 It may have occurred, but I</p> <p>18 don't specifically recall that being done.</p> <p>19 Q Does Enzon have any idea where</p> <p>20 Dr. Clark got the idea to use ester, epoxy,</p> <p>21 carboxyl, hydroxyl or carbohydrate groups to</p> <p>22 link PEG and ADI?</p> <p>23 MR. SIEM: Objection to form.</p> <p>24 A Well, again, I can't read</p> <p>25 somebody else's mind, but the use of linkers</p>

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David Filpula

<p style="text-align: right;">Page 182</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 and linkages like this is kind of textbook.</p> <p>3 It's, you know, the type of</p> <p>4 linkages that one uses for a variety of</p> <p>5 conjugations.</p> <p>6 So I mean he could read a</p> <p>7 textbook and find most of this, I guess, or an</p> <p>8 article in the literature.</p> <p>9 Q The use of ester, epoxy,</p> <p>10 carboxyl, hydroxyl and carbohydrate groups for</p> <p>11 linking PEG and ADI isn't proprietary to Enzon,</p> <p>12 is it?</p> <p>13 MR. SIEM: Objection to form.</p> <p>14 A That I think, when you say</p> <p>15 proprietary, that gets into a legal issue, and</p> <p>16 I can only address factual issues as a research</p> <p>17 scientist, I am not an attorney.</p> <p>18 Q Well, on that basis can you</p> <p>19 answer my question?</p> <p>20 MR. SIEM: Objection to form.</p> <p>21 A And again, the question was</p> <p>22 whether it was proprietary? No, I can't answer</p> <p>23 that.</p> <p>24 Q You don't know whether or not</p> <p>25 the use of those linkers to link PEG and ADI</p>	<p style="text-align: right;">Page 184</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 to whether or not Takaku -- you are aware of</p> <p>3 the publications of Takaku on ADI, correct?</p> <p>4 A There were previous publications</p> <p>5 on ADI to 1996, you've mentioned the years in</p> <p>6 the early '90s and indeed in the early '90s</p> <p>7 there were significant publications on ADI.</p> <p>8 You mentioned one specific</p> <p>9 author's name, Takaku, that sounds familiar,</p> <p>10 but again without seeing the article and</p> <p>11 refreshing my memory as to his article, I can</p> <p>12 simply say that there have been publications on</p> <p>13 the use of ADI in the literature in the early</p> <p>14 '90s and it was -- there was evidence provided</p> <p>15 that they had anti-cancer effects.</p> <p>16 Q Do you have an understanding as</p> <p>17 to whether in that early '90s time period it</p> <p>18 has also been published to put PEG on ADI?</p> <p>19 MR. SIEM: Objection to form.</p> <p>20 A Yes, there was an article, I'm</p> <p>21 not sure of the year, that described PEGylation</p> <p>22 of an ADI and it's anti -- I believe it</p> <p>23 included some anti-tumor effects, at least in</p> <p>24 cell culture.</p> <p>25 Q Would it be consistent with your</p>
<p style="text-align: right;">Page 183</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 was proprietary to Enzon?</p> <p>3 A No, I don't know.</p> <p>4 Q You mentioned that you could</p> <p>5 find them in a textbook, though, right?</p> <p>6 A Yes, but it's all about timing,</p> <p>7 when the textbook came out.</p> <p>8 Q Could you have found them in a</p> <p>9 textbook in 1996?</p> <p>10 A I'm not certain, perhaps.</p> <p>11 Q The use of ADI as a treatment</p> <p>12 for cancer was in the public domain before</p> <p>13 Enzon got involved in using ADI, correct?</p> <p>14 A I'm not certain of that, but the</p> <p>15 idea of using arginine deprivation to treat</p> <p>16 cancers has been around quite a while.</p> <p>17 Q Isn't it the case that Takaku</p> <p>18 published in 1992 on the use of ADI for</p> <p>19 mycoplasma to treat cancer?</p> <p>20 MR. SIEM: Objection to form.</p> <p>21 A Again, I don't have the document</p> <p>22 in front of me, so I don't know how to treat to</p> <p>23 that.</p> <p>24 Q Well when you got involved</p> <p>25 working with ADI, was it your understanding as</p>	<p style="text-align: right;">Page 185</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 recollection that publication came out in 1993?</p> <p>3 A Possibly.</p> <p>4 Q How did Enzon get involved</p> <p>5 initially in using ADI?</p> <p>6 A The history behind that even</p> <p>7 predates me, and I've been with the company a</p> <p>8 long time.</p> <p>9 The founder of the company, the</p> <p>10 founders of the company, Frank Davis and Abe</p> <p>11 Abakowski had an interest all along in using</p> <p>12 PEGylated enzymes to deplete essential amino</p> <p>13 acids and thereby treat cancers.</p> <p>14 One of the enzymes that they</p> <p>15 worked on, I believe, while they were still in</p> <p>16 academia at Rutgers was N-arginase, arginase</p> <p>17 depletes arginine from the blood or from serum</p> <p>18 or from aqueous solutions for that matter,</p> <p>19 through a similar but not identical mechanism.</p> <p>20 They worked on PEGylating</p> <p>21 arginase back then. That gradually led to a</p> <p>22 PEGylation program on pseudomonas ADI and then</p> <p>23 we have discussed the further evolution to the</p> <p>24 mycoplasma program.</p> <p>25 Q Do you remember anyone at Enzon</p>

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8/4/2005

Enzon Pharmaceuticals Inc. v. Phoenix Pharmacologics  
Confidential Pursuant To Protective Order

David Filpula

<p style="text-align: right;">Page 186</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 expressing skepticism over the use of PEG</p> <p>3 polymers having molecular weight greater than</p> <p>4 12,000 for PEGylating ADI?</p> <p>5 A No, I don't recall that.</p> <p>6 Q Dr. Filpula, in the '738 patent</p> <p>7 you have there, if you could turn to the last</p> <p>8 page of it, in claim 3 there is a reference in</p> <p>9 the second line to a succinimidyl succinate</p> <p>10 group, do you see that?</p> <p>11 A Yes.</p> <p>12 Q Did Enzon use that group to link</p> <p>13 PEG and ADI?</p> <p>14 A It's possible, the succinimidyl</p> <p>15 succinate group or as we call it the SS group</p> <p>16 is one that we have used extensively at Enzon</p> <p>17 over the years, in fact two of our marketed</p> <p>18 products use that chemistry.</p> <p>19 It would be unsurprising to me</p> <p>20 if we explored that chemistry, I don't</p> <p>21 specifically recall if we did or not, only that</p> <p>22 it would be unsurprising.</p> <p>23 Q Can you point me to any document</p> <p>24 in Enzon's document production to Phoenix that</p> <p>25 discusses the use of the succinimidyl succinate</p>	<p style="text-align: right;">Page 188</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 Q And you're not aware of any work</p> <p>3 apart from what's referenced in the documents</p> <p>4 directed to the use of that linker to link PEG</p> <p>5 and ADI?</p> <p>6 MR. SIEM: Objection to form.</p> <p>7 A I don't recall that.</p> <p>8 Q Does Enzon know where Dr. Clark</p> <p>9 got the idea to use the succinimidyl succinate</p> <p>10 linker to link PEG and ADI?</p> <p>11 MR. SIEM: Objection to form.</p> <p>12 A Again, I can't read someone</p> <p>13 else's mind, however given the complete</p> <p>14 knowledge that Mike had of the enzyme program</p> <p>15 employing a variety of PEG linkers and the fact</p> <p>16 that Enzon extensively worked on SS PEG during</p> <p>17 the two year period that he was there on other</p> <p>18 projects, I would have to assume that he would</p> <p>19 have been very well exposed to SS PEG during</p> <p>20 his employment.</p> <p>21 Q Was, the fact that Enzon was</p> <p>22 using SS PEG is something that was confidential</p> <p>23 to the company in that time period?</p> <p>24 MR. SIEM: Objection to form.</p> <p>25 A I believe that the use of SS PEG</p>
<p style="text-align: right;">Page 187</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 group to link PEG and ADI?</p> <p>3 MR. SIEM: Objection to form.</p> <p>4 A As I mentioned, I don't recall</p> <p>5 seeing specific mention of using the SS linker</p> <p>6 together with PEGylation of ADI, we would</p> <p>7 certainly have been extremely well aware of the</p> <p>8 potential to do so if we wished to for the very</p> <p>9 reasons I've stated.</p> <p>10 The SS linker is okay, we felt</p> <p>11 that the SC linker has superior features</p> <p>12 overall and probably chose to focus more of the</p> <p>13 work on that linker for that reason.</p> <p>14 Q Was the SS linker known in the</p> <p>15 literature prior to 1994?</p> <p>16 A Yes, I believe so.</p> <p>17 Q There is another linker</p> <p>18 mentioned on the next line, the succinimidyl</p> <p>19 succinamide, do you see that there?</p> <p>20 A Yes.</p> <p>21 Q Are you aware of any work at</p> <p>22 Enzon to use that linker to link PEG and ADI?</p> <p>23 A I don't recall seeing that</p> <p>24 specific linker in the documents that I</p> <p>25 reviewed.</p>	<p style="text-align: right;">Page 189</p> <p>1 DAVID RAY FILPULA - CONFIDENTIAL</p> <p>2 on some projects was publicly known.</p> <p>3 Q With respect to the succinimidyl</p> <p>4 succinamide, does Enzon have any idea where Dr.</p> <p>5 Clark got the idea to use that to link PEG and</p> <p>6 ADI?</p> <p>7 MR. SIEM: Objection to form.</p> <p>8 A Again, it would be a somewhat</p> <p>9 similar answer, the linkers that Enzon used</p> <p>10 during that period of time were various, Enzon</p> <p>11 is really or especially then was and today as</p> <p>12 well, I believe, most especially in the '90s</p> <p>13 was the place to be for PEGylation.</p> <p>14 We were the PEGylation experts.</p> <p>15 And I think we are still are,</p> <p>16 but certainly then there was just no question.</p> <p>17 Mike was exposed to the best</p> <p>18 PEGylation programs anywhere that I know of,</p> <p>19 and I would guess he would be able to learn</p> <p>20 more about a variety of linkers, and indeed</p> <p>21 would be someone would would want to learn more</p> <p>22 about the very company that he works for.</p> <p>23 Q But the fact that Enzon used a</p> <p>24 variety of linkers wasn't a matter that Enzon</p> <p>25 kept in confidence, was it?</p>

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